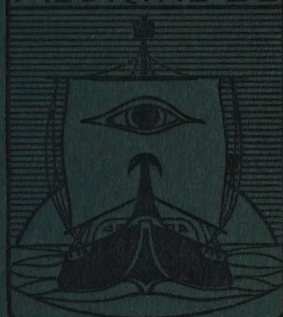


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ANNALS

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III.—Intravenous Injections of Quinine Bihydrochloride

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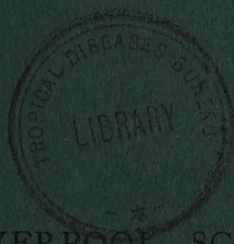
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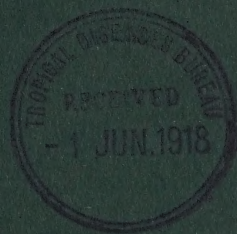
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REPRINTED FROM THE
ANNALS OF TROPICAL MEDICINE AND PARASITOLOGY
Vol. XI, No. 2, August, 1917



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STUDIES IN THE TREATMENT OF MALARIA

III. INTRAVENOUS INJECTIONS OF QUININE BIHYDROCHLORIDE

BY

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(Received for publication 7 May, 1917)

Baccelli (1890) was apparently the first to use this method* in the treatment of malaria. He concludes that in very severe cases where other channels of absorption do not suffice, it is the most energetic, most certain, and quickest mode of therapy. This form of treatment has been much used since Baccelli's time, but so far as we are aware, no series of cases has been recorded where the clinical results have been controlled by systematic microscopical examina-

* He used the following formula :—Chininhydrochlorat 1·00 g. ; Chlornatrium 0·75 g.;
Destillirtes Wasser 10·00 g.

tions. In this paper we propose to give the results of treating thirty cases of malaria by intravenous injections of quinine bihydrochloride with a view to furnishing these data.

The solution used for injection was a 10 per cent. solution of bihydrochloride of quinine in normal saline. In Baccelli's formula, if correctly given, the strength of the salt solution was 7.5 per cent.

SIMPLE TERTIAN MALARIA (Cases 43-63)

Single injections were given in eight cases. In seven of these the amount of quinine injected was grns. 15, in the other, grns. 10. The detailed results are given in Tables I and II.

In the following temperature charts and tables

Q.V. = intravenous injection of quinine bihydrochloride.

gr. = grains of quinine bihydrochloride.

T. = simple tertian trophozoites or schizonts.

G. = simple tertian gametes.

t. = malignant tertian trophozoites or schizonts.

cr. = malignant tertian gametes.

Neg. = No parasites found.

* = quinine sulphate orally given daily.

The results were similar in all cases. The temperature fell to normal in one to three days, and parasites disappeared from the cutaneous blood in two to five days.

Relapses. Six of the eight cases relapsed. Parasites reappeared in 8-14 days. Febrile paroxysms recurred on an average in 15 days (minimum 10, maximum 20). Of the remaining two cases, one was given quinine orally on the fourth day, and the other died of cerebral haemorrhage of undetermined nature on the tenth day.

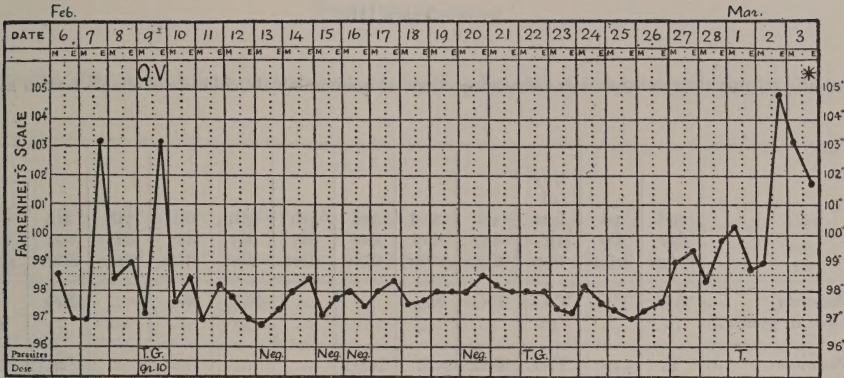
As the temperature charts of this series of cases were similar, and presented no points of special interest, two only are reproduced. (Charts 43 and 48).

TABLE II.

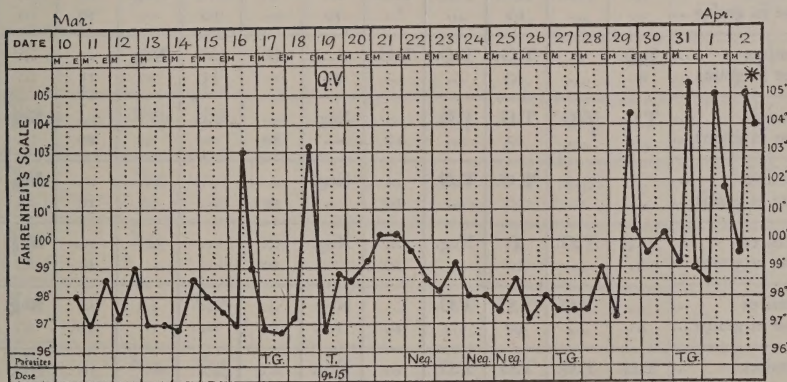
Summary of results of a single intravenous injection of quinine bihydrochloride in simple tertian malaria.

Number of case	Temperature fell to normal in — days after injection	Parasites disappeared from cutaneous blood in — days after injection	Parasitic relapse occurred in — days after injection	Febrile relapse (above 100° F.) occurred in — days after injection	Remarks
43	1	1 - 4	12 - 13	20	—
44	1	2 - 3	9 - 13	16	—
45	1	3	4 - 8	—	Quinine sulphate orally on ninth day
46	1	2	9 - 10	10	—
47	same day	2 - 3	11 - 14	20	—
48	3	1 - 3	7 - 8	10	—
49	—	4 - 5	—	—	Died of cerebral haemorrhage on tenth day after injection
50	1	2	—	—	Quinine sulphate orally on fifth day

CASE 43.



CASE 48.



Multiple injections were given in thirteen cases, 5 in one case and 6 in twelve. The injections were given on Mondays, Wednesdays and Fridays. As a rule grns. 10 were given at each injection, but on a few occasions grns. 15. The detailed results are given in Tables III and IV.

TABLE III.

Parasitic records after multiple intravenous injections of quinine bihydrochloride in simple tertian malaria.

Number of Case		2nd day before	1st day before	Day of first injection	1st day after	2nd day after	3rd day after	4th day after	5th day after	6th day after	7th day after	8th day after	9th day after	10th day after	11th day after
51	Parasites ... Dose in grains ...	T.G. ...	T.G. ...	T.G. 10	T.G. ...	Neg. 10	...	...	Neg. 10	Neg. ...	...	Neg. ...	...	...	...
52	Parasites ... Dose in grains ...	T. ...	...	T.G. 15	T.G. ...	...	Neg. 10	...	...	...	...	(cr.) ...	...	...	Neg. 10
53	Parasites ... Dose in grains ...	T.G. ...	T.G. ...	T.G. 10	...	...	...	T.G. 10	...	Neg. 10	...	...	...	...	T. ...
54	Parasites ... Dose in grains ...	T.G. ...	T.G. ...	T.G. 10	T.G. ...	...	...	...	...	T. 10	...	Neg. ...	...	...	...
55	Parasites ... Dose in grains ...	...	T.G. ...	T.G. 10	T.G. ...	T.G. 10	...	T. ...	...	Neg. 10	...	...	...	...	Neg. ...
56	Parasites ... Dose in grains ...	T.G. ...	...	T.G. 10	T.G. ...	T.G. ...	...	G. 10	...	Neg. 15	...	...	...	...	Neg. ...
57	Parasites ... Dose in grains ...	T.G. ...	T.G. ...	T.G. 10	T.G. ...	...	Neg. 10	...	...	...	...	Neg. ...	...	Neg. 5	...
58	Parasites ... Dose in grains ...	...	...	T.G. 10	T.G. ...	...	Neg. 10	...	...	...	...	Neg. ...	...	Neg. 10	...
59	Parasites ... Dose in grains ...	...	T.G. ...	T. 10	Neg. ...	...	Neg. 10	...	...	...	...	Neg. 10	...	Neg. 10	...
60	Parasites ... Dose in grains ...	...	T.G. ...	T.G. 10	T.G. ...	...	Neg. 10	...	...	...	...	Neg. ...	...	Neg. 10	...
61	Parasites ... Dose in grains ...	T.G. ...	T.G. ...	T.G. 10	T.G. ...	...	Neg. 10	...	...	...	...	Neg. ...	...	Neg. 10	...
62	Parasites ... Dose in grains ...	T.G. ...	T.G. ...	T.G. 10	T.G. ...	...	Neg. 10	...	...	...	...	Neg. ...	...	Neg. 10	...
63	Parasites ... Dose in grains ...	...	...	T.G. 10	T.G. ...	...	Neg. 10	...	...	...	...	Neg. ...	...	Neg. 10	...

TABLE III.—continued

Parasitic records after multiple intravenous injections of quinine bihydrochloride in simple tertian malaria—cont.

	13th day after	14th day after	15th day after	16th day after	17th day after	18th day after	19th day after	20th day after	21st day after	22nd day after	23rd day after	24th day after	25th day after	26th day after	27th day after	28th day after	29th day after
...	Neg.	...	Neg.	...	...	T.G.	...	...	...	...	...	...	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	...	...	(cr.)	...	Neg.	...	...	...	Neg.	Neg.	...	Neg.	...	...	...	...	T.G.
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	T	T.	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	Neg.	...	Neg.	...	...	...	...	Neg.	...	T.G.	...	...	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	Neg.	...	Neg.	...	...	Neg.	...	T.	...	...	...	...	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	Neg.	...	...	...	Neg.	Neg.	...	...	Neg.	...	...	T.	T.G.	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	...	...	Neg.	...	Neg.	Neg.	...	...	...	Neg.	...	Neg.	...	...	...	...	Neg.
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	...	...	Neg.	...	Neg.	...	...	...	...	T.G.	T.G.	T.G.	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	*	...	...	...	...	...
...	...	...	Neg.	...	Neg.	...	...	...	...	...	T.	T.	T.G.	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	...	*	...	...	...	...
...	...	...	Neg.	...	...	Neg.	...	...	...	T.	...	T.G.	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	...	*	...	...	...	...
...	...	...	Neg.	...	Neg.	Neg.	...	...	...	T.	...	T.G.	T.G.	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	...	...	Neg.	...	Neg.	...	...	...	...	T.G.	...	...	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	...	...	Neg.	...	Neg.	Neg.	...	...	...	T.G.	...	T.G.	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	...	*	...	...	...	...

TABLE IV.

Summary of results of multiple intravenous injections of quinine bihydrochloride in simple tertian malaria.

Number of case	Number of injections	Temperature fell to normal after — injections	Parasites disappeared from cutaneous blood after — injections	Parasitic relapse occurred in — days after first injection	Febrile relapse (above 100° F.) occurred in — days after first injection	Parasitic relapse occurred in — days after last injection	Febrile relapse (above 100° F.) occurred in — days after last injection	Remarks
51	5	2	1	16 - 18	18	7 - 9	9	—
52	6	1	2	25 - 29	29	14 - 18	18	Crescents present during treatment
53	6	1	...	...	14	...	2	Parasites present except on one examination
54	6	3	4	21 - 22	22	9 - 10	10	—
55	6	1	3	19 - 20	...	7 - 8	...	Quinine sulphate 20 gr. orally on 20th day
56	6	1	3	22 - 24	23	10 - 12	11	—
57	6	1	2	...	...	...	...	No relapse in 2½ months
58	6	1	2	18 - 22	22	7 - 11	11	—
59	6	1	1	18 - 23	25	7 - 12	14	—
60	6	1	2	19 - 22	22	8 - 11	11	—
61	6	1	2	19 - 22	25	8 - 11	14	—
62	6	1	2	18 - 22	23	7 - 11	12	—
63	6	1	2	19 - 22	22	8 - 11	11	—

In one case (53) the treatment did not cause the disappearance of parasites from the blood, but as shown in Chart 53 the febrile paroxysms were controlled.

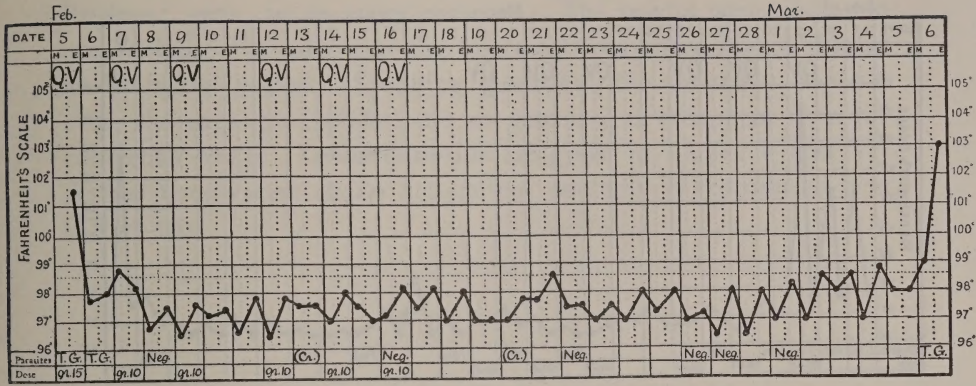
In another case (57) the temperature fell to normal after the first injection, parasites disappeared from the blood after the second injection, and there was no relapse for an observation period of two and a half months.

In the remaining eleven cases the results, which were similar to one another, were as follows: The temperature fell to normal after one to three injections; the parasites disappeared from the blood after one to four injections.

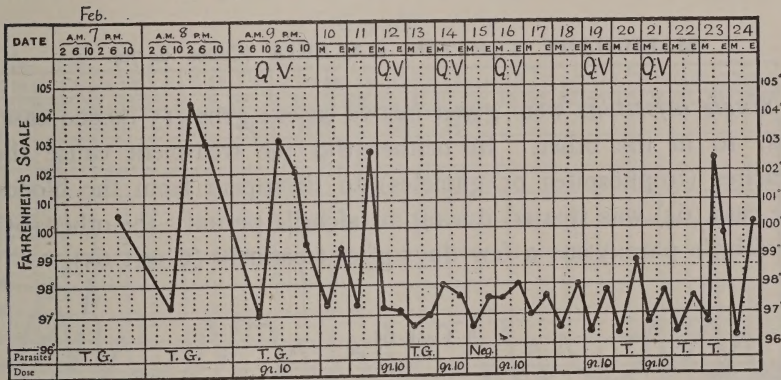
Relapses. All of the eleven cases relapsed. Parasites reappeared in 8-18 days. Febrile paroxysms recurred on an average in 11 days (minimum 11, maximum 15).

As the temperature charts of these eleven cases were similar, three only are reproduced here (Charts 52, 54 and 62).

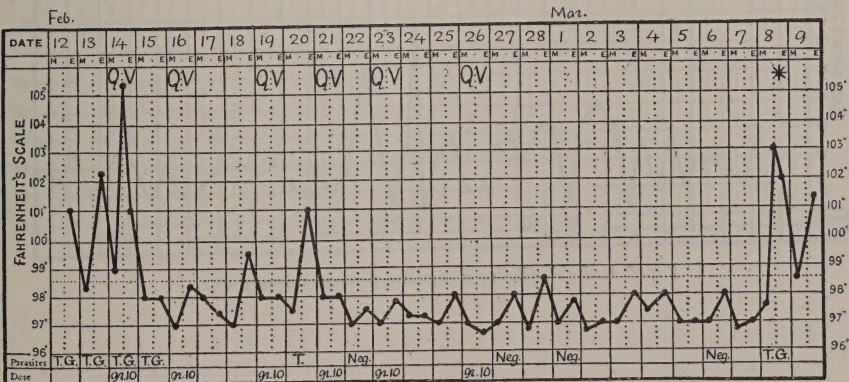
CASE 52.



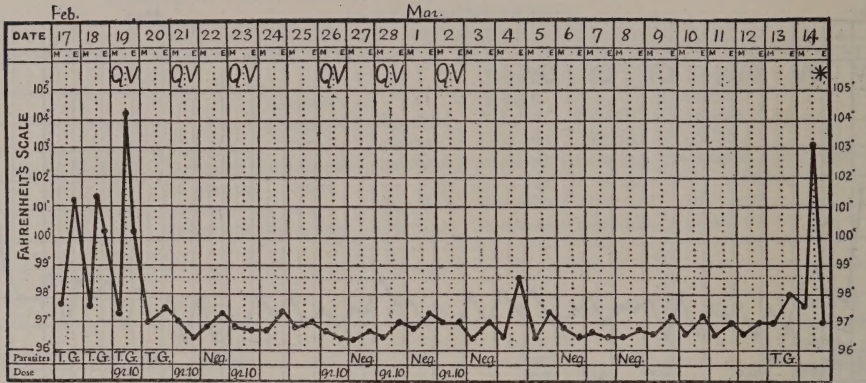
CASE 53.



CASE 54.



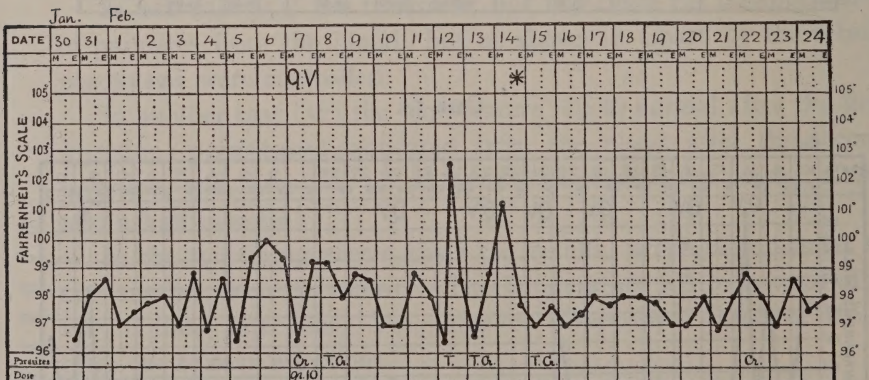
CASE 62.



MALIGNANT TERTIAN MALARIA (Cases 64-70)

Single injections were given in two cases: grns. 15 in one case, grns. 10 in the other. In neither did the treatment cause the parasites (trophozoites or gametes) to disappear from the blood. One case (64) was treated during an afebrile period; the other (65) had febrile paroxysms a few days after treatment (Chart 65).

CASE 65.



For *T* read *t* signifying malignant tertian trophozoites.

Multiple injections were given in five cases: 4 in one case, and 6 in four. The injections were given on Mondays, Wednesdays and Fridays; grns. 10 on every occasion. The results were similar to one another. In each case the treatment was administered during an apyrexial period. Speaking generally, the treatment did not cause the parasites (trophozoites or gametes) to disappear from the cutaneous blood. Detailed results are given in Tables V and VI. As the temperature charts are similar, one only is reproduced here (Chart 68).

CASE 68.

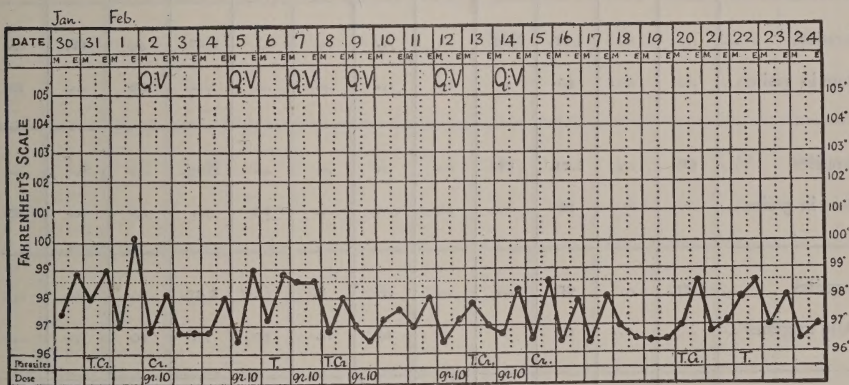


TABLE V.

Parasitic records after intravenous injections of quinine bihydrochloride in malignant tertian malaria.

Number of Case		2nd day before	1st day before	Day of first injection	1st day after	2nd day after	3rd day after	4th day after	5th day after	6th day after	7th day after	8th day after	9th day after	10th day after	11th day after
64	Parasites ...	t.	t.	t.	t.	t.	t.	t.cr.	...	...	...	...	...	t.cr.	...
	Dose in grains ...	...	...	15	...	...	...	...	...	...	...	...	...	...	...
65	Parasites ...	...	...	cr.	t.cr.	...	...	...	t.	t.cr.	...	t.cr.	...	...	...
	Dose in grains ...	...	...	10	...	...	...	...	...	...	*	...	...	...	...
66	Parasites ...	...	...	t.cr.	Neg.	...	...	...	...	t.cr.	...	cr.	...	...	...
	Dose in grains ...	...	...	10	...	10	...	...	...	...	10	...	10	...	...
67	Parasites ...	cr.	...	t.cr.	cr.	...	...	...	...	Neg.	...	t.	...	...	...
	Dose in grains ...	...	...	10	...	10	...	...	10	...	...	...	10	...	...
68	Parasites ...	t.cr.	...	cr.	...	...	...	t.	...	t.cr.	...	...	...	...	t.cr.
	Dose in grains ...	...	...	10	...	...	10	...	10	...	10	...	...	10	...
69	Parasites ...	...	...	cr.	Neg.	...	...	...	...	Neg.	...	Neg.	...	...	...
	Dose in grains ...	...	...	10	...	10	...	...	10	...	10	...	10	...	...
70	Parasites ...	t.cr.	...	t.cr.	cr.	...	...	...	...	cr.	...	cr.	...	...	...
	Dose in grains ...	...	...	10	...	10	...	...	10	...	10	...	10	...	...

[illegible]

TABLE VI.

Summary of results of intravenous injections of quinine bihydrochloride in malignant tertian malaria.

Number of case	Number of injections	Remarks
64	1	Treatment during an apyrexial period. Trophozoites and gametes persist
65	1	Fever unaffected: <i>vide</i> Chart. Trophozoites and gametes persist
66	4	Treatment during apyrexial period. Gametes persist
67	6	Treatment during apyrexial period. Trophozoites and gametes persist
68	6	Treatment during apyrexial period. Trophozoites and gametes persist
69	6	Treatment during apyrexial period. Gametes disappear, but reappear 29 days after last injection
70	6	Treatment during apyrexial period. Trophozoites disappear, gametes persist

DOUBLE INFECTIONS WITH SIMPLE AND MALIGNANT TERTIAN MALARIA (Cases 71 and 72)

Although some of the cases of simple tertian malaria recorded above showed crescents from time to time, these two cases are grouped separately because at the time of treatment both trophozoites and gametes of *P. vivax* and *P. falciparum* were present.

The detailed results are given in Tables VII and VIII.

TABLE VII.

Summary of results of intravenous injections of quinine bihydrochloride in double infections with simple and malignant tertian malaria.

Number of case	Number of injections	Temperature fell to normal after — injections	Parasites disappeared from cutaneous blood after — injections	Parasitic relapse occurred in — days after first injection	Febrile relapse (above 100° F.) occurred in — days after first injection	Parasitic relapse occurred in — days after last injection	Febrile relapse (above 100° F.) occurred in — days after last injection	Remarks
71	6	2	5	23-24	23	11-12	11	—
72	6	1	2	18	19	6	7	—

TABLE VIII.

Parasitic records after intravenous injections of quinine bihydrochloride in double infections with simple and malignant tertian malaria.

Number of Case		2nd day before	1st day before	Day of first injection	1st day after	2nd day after	3rd day after	4th day after	5th day after	6th day after	7th day after	8th day after	9th day after	10th day after	11th day after
71	<i>P. vivax</i> ...	T.G.	T.G.	T.G.	T.G.	T.G.	...	T.G.	...	T.	...	G.	...	...	...
	<i>P. falciparum</i> ...	...	t.cr.	t.cr.	Neg.	Neg.	...	Neg.	...	Neg.	...	Neg.	...	...	...
	Dose in grains ...	...	...	10	...	10	...	...	10	...	10	...	10	...	...
72	<i>P. vivax</i> ...	...	T.G.	T.G.	T.G.	T.	...	Neg	...	Neg.	...	...	...	...	Neg.
	<i>P. falciparum</i> ...	...	...	t.cr.	...	cr.	...	Neg.	...	Neg.	...	...	...	...	Neg.
	Dose in grains ...	...	...	10	...	...	10	...	10	...	15	...	...	15	...

TABLE VIII.—continued.

Parasitic records after intravenous injections of quinine bihydrochloride in double infections with simple and malignant tertian malaria.—*cont.*

[illegible]

EFFECTS OF THE INJECTIONS

In this series of 127 injections, thrombosis occurred in four patients. Two of these had thrombosis in each arm, and two in one arm only. There was no other symptom worthy of note.

CONCLUSIONS

1. In simple tertian malaria, intravenous injections of quinine bihydrochloride in the doses used (grns. 10-15)—either one or a series of six—effect a temporary cure (i.e., cessation of febrile paroxysms and disappearance of parasites from the cutaneous blood). Relapses occur after approximately the same period from the end of treatment, whether one or six injections have been given.
2. In malignant tertian malaria, neither a single nor a series of six injections, in the doses used (grns. 10-15) causes the disappearance of parasites (trophozoites or gametes) from the cutaneous blood.

POSTSCRIPT

Since the above paper was written, an article by Soulié (1917) has appeared, in which he states that, using intravenous injections of quinine-urethane—two injections of 1 gramme each three times a week for a period of four to six weeks—he has effected cures in about sixty cases, relapses being exceptional. The period of observation after cessation of treatment is not given, but it is stated that the cases were followed.

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- BACCELLI, G. (1890). *Berl. Klin. Woch.*, p. 489.
SOULIÉ, H. (1917). *Bull. Soc. Path. Exot.*, Vol. X, p. 217.



